

## Title (en)

TISSUE REPAIR BY MODULATION OF BETA-1 INTEGRIN BIOLOGICAL FUNCTION

## Title (de)

GEWEBEREPARATUR DURCH MODULATION DER BIOLOGISCHEN FUNKTION VON BETA-1-INTEGRIN

## Title (fr)

REPARATION DE TISSUS VIA LA MODULATION DE LA FONCTION BIOLOGIQUE DE L'INTEGRINE BETA-1

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## Application

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## Abstract (en)

The present invention provides methods and novel compounds for facilitating tissue repair and regeneration when the extracellular matrix is damaged. Specifically, binding of the beta-1 integrin is shown to provide a modulation of its functional activity resulting in up regulation of extracellular matrix anabolism. The invention therefore provides a method and novel compounds which can facilitate tissue regeneration in many systems such as the lung, skin, liver and bone. In particular, the binding of the JB1a antibody to a site of amino acid residues 82 to 87 of the mature beta-1 integrin is shown to be particularly effective in mediating the described tissue repair effect.

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## Citation (applicant)

- US 5225539 A 19930706 - WINTER GREGORY P [GB]
- EP 0120694 A2 19841003 - CELLTECH LTD [GB]
- EP 0125023 A1 19841114 - GENENTECH INC [US], et al
- US 9209965 W 19921120
- WO 9413804 A1 19940623 - CAMBRIDGE ANTIBODY TECH [GB], et al
- EP 04768934 A 20041018
- GENNARO, A.R.: "Remington's Pharmaceutical Sciences", 15 December 2000, LIPPINCOTT WILLIAMS & WILKINS
- ANSEL, H.C. ET AL.: "Pharmaceutical Dosage Forms and Drug Delivery Systems. 7th ed.", 1999, LIPPINCOTT WILLIAMS & WILKINS
- ALBUQUERQUE ML; FLOZAK AS, J CELL PHYSIOL, vol. 195, 2003, pages 50 - 60
- ASPBERG A ET AL., J BIOL CHEM, vol. 274, 1999, pages 20444 - 20449
- ASPBERG A ET AL., PROC NATL ACAD SCI U S A, vol. 94, 1997, pages 10116 - 10121
- AUMAILLEY M; GAYRAUD B, J MOL MED, vol. 76, 1998, pages 253 - 265
- AVIEZER D ET AL., CELL, vol. 79, 1994, pages 1005 - 1013
- BADGER AM ET AL., ARTHRITIS RHEUM, vol. 44, 2001, pages 128 - 137
- BANG OS ET AL., BIOCHEM BIOPHYS RES COMMUN, vol. 278, 2000, pages 522 - 529
- BARNES PJ, ANNU REV MED, vol. 54, 2003, pages 113 - 129
- BENSADOUN ES; BURKE AK; HOGG JC; ROBERTS CR: "Proteoglycan deposition in pulmonary fibrosis", AM J RESPIR CRIT CARE MED, vol. 154, 1996, pages 1819 - 1828, XP008135909
- BINGLEY JA ET AL., J VASE SURG, vol. 28, 1998, pages 308 - 318
- BIRD RE ET AL., SCIENCE, vol. 242, 1988, pages 423 - 426
- BOZZO C ET AL., MOL CELL NEUROSCI, vol. 25, 2004, pages 1 - 8
- BROWN CT ET AL., J BIOL CHEM, vol. 274, 1999, pages 7111 - 7119
- BROWN JC ET AL., EUR J BIOCHEM, vol. 250, 1997, pages 39 - 46
- CALVERLEY P; BELLAMY D, THORAX, vol. 55, 2000, pages 78 - 82
- CAO L ET AL., MATRIX BIOL, vol. 18, 1999, pages 343 - 355
- CAWSTON T ET AL., NOVARTIS FOUND SYMP, vol. 234, 2001, pages 205 - 218
- CHAKRAVARTI S ET AL., J IOL CHEM, vol. 270, 1995, pages 404 - 409
- COSTELL M ET AL., J CELL BIOL, vol. 147, 1999, pages 1109 - 1122
- COUCHMAN JR ET AL., KIDNEY INT, vol. 43, 1993, pages 79 - 84
- CURLEY GP ET AL., CELL MOL LIFE SCI, vol. 56, 1999, pages 427 - 441
- DOLHNIKOFF M ET AL., AM J RESPIR CELL MOL BIOL, vol. 19, 1998, pages 582 - 587
- DUNLEVY JR; HASSELL JR: "In: Proteoglycans: Structure, Biology and Molecular Interactions", 2000, MARCEL DEKKER, article "Heparan Sulfate Proteoglycans in Basement Membranes: Perlecan, Agrin, and Collagen XVIII", pages: 275 - 326
- EBIHARA T; VENKATESAN N; TANAKA R; LUDWIG S. ET AL., AM J RESPIR CRIT CARE MED, vol. 162, 2000, pages 1569 - 1576
- ELBERT KJ ET AL., PHARM RES, vol. 16, 1999, pages 601 - 608
- ETTNER N ET AL., FEBS LETT, vol. 430, 1998, pages 217 - 221
- EVANKO SP ET AL., ARTERIOSCLER THROMB VASE BIOL, vol. 19, 1999, pages 1004 - 1013
- FESTUCCIA C ET AL., EXP CELL RES, vol. 280, 2002, pages 1 - 11
- FREEDMAN GM., GERIATRICS, vol. 57, 2002, pages 36 - 41
- FUKI IV ET AL., J BIOL CHEM, vol. 275, 2000, pages 25742 - 25750
- GALLAGHER JT., BIOCHEM SOC TRANS, vol. 25, 1997, pages 1206 - 1209
- GOLDSMITH EC ET AL., AM J PHYSIOL HEART CIRC HYSIOL, vol. 284, 2003, pages H2227 - H2234
- GOODISON S ET AL., OL PATHOL, vol. 52, 1999, pages 189 - 196
- GREEN SJ ET AL., J CELL SCI, vol. 90, 1988, pages 145 - 156
- GREEN SJ; UNDERHILL CB, J CELL PHYSIOL, vol. 134, 1988, pages 376 - 386
- GROFFEN AJ ET AL., EUR J BIOCHEM, vol. 254, 1998, pages 123 - 128
- GROSE R ET AL., DEVELOPMENT, vol. 129, 2002, pages 2303 - 2315

- HALFTER W ET AL., J BIOL CHEM, vol. 273, 1998, pages 25404 - 25412
- HANTOS Z ET AL., J APPL PHYSIOL, vol. 73, 1992, pages 427 - 433
- HANTOS Z ET AL., J APPL PHYSIOL, vol. 68, 1990, pages 849 - 860
- HANTOS Z ET AL., J APPL PHYSIOL, vol. 72, 1992, pages 168 - 178
- HARALSON MA; HASSELL JR.: "Extracellular Matrix: A practical approach", 1995, OXFORD UNIVERSITY PRESS, article "The extracellular matrix-an overview", pages: 1 - 30
- HARTWELL LH ET AL., NATURE, vol. 402, 1999, pages C47 - C52
- HASSELL JR ET AL., PROC NATL ACAD SCI U S A, vol. 77, 1980, pages 4494 - 4498
- HIROSE J ET AL., J BIOL CHEM, 2000
- HOLLINGER M.: "Flight to duty", AM J NURS, vol. 101, 2001, pages 15
- HOPF M ET AL., EUR J BIOCHEM, vol. 259, 1999, pages 917 - 925
- HUMPHRIES MJ., J CELL SCI, vol. 97, 1990, pages 585 - 592
- HUMPHRIES MJ., TRENDS PHARMACOL SCI, vol. 21, 2000, pages 29 - 32
- HUSTON JS ET AL., PROC NATL ACAD SCI U S A, vol. 85, 1988, pages 5879 - 5883
- IOZZO RV., MATRIX BIOL, vol. 14, 1994, pages 203 - 208
- IOZZO RV., ANNU REV BIOCHEM, vol. 67, 1998, pages 609 - 652
- JACKSON RL ET AL., PHYSIOL REV, vol. 71, 1991, pages 481 - 539
- JUUL SE ET AL., AM J RESPIR CELL MOL BIOL, vol. 8, 1993, pages 299 - 310
- KAWASHIMA H ET AL., J BIOL CHEM, vol. 275, 2000, pages 35448 - 35456
- KAWASHIMA H ET AL., INT IMMUNOL, vol. 11, 1999, pages 393 - 405
- KENNEL SJ ET AL., J CELL SCI, vol. 104, 1993, pages 373 - 382
- KNIGHT D., IMMUNOL CELL BIOL, vol. 79, 2001, pages 160 - 164
- KOENIG A ET AL., J CLIN INVEST, vol. 101, 1998, pages 877 - 889
- KRANEVELD AD ET AL., J ALLERGY CLIN IMMUNOL, vol. 100, 1997, pages 242 - 250
- LEBARON RG ET AL., J BIOL CHEM, vol. 267, 1992, pages 10003 - 10010
- LEIR SH ET AL., AM J PHYSIOL LUNG CELL MOL PHYSIOL, vol. 278, 2000, pages L1129 - L1137
- LEMIRE JM ET AL., ARTERIOSCLER THROMB VASE BIOL, vol. 19, 1999, pages 1630 - 1639
- LEVKAU B ET AL., CELL DEATH DIFFER, vol. 9, 2002, pages 1360 - 1367
- LI YF ET AL., FEBS LETT, vol. 444, 1999, pages 201 - 205
- LITTLE CB ET AL., MATRIX BIOL, vol. 21, 2002, pages 271 - 288
- LOFTUS I ET AL., BR J SURG, vol. 89, 2002, pages 680 - 694
- MANIOTIS ET AL., PROC NATL ACAD SCI U S A, vol. 94, 1997, pages 849 - 854
- MANISCALCO WM; CAMPBELL MH, AM J PHYSIOL, vol. 263, 1992, pages L348 - L356
- MENGSHOL JA ET AL., ARTHRITIS RHEUM, vol. 46, 2002, pages 13 - 20
- MILNE AA; PIPER PJ, EUR J PHARMACOL, vol. 282, 1995, pages 243 - 249
- MOULD AP ET AL., J BIOL CHEM, 2003
- MURDOCH AD ET AL., J HISTOCHEM CYTOCHEM, vol. 42, 1994, pages 239 - 249
- MURDOCH A ET AL., J HISTOCHEM CYTOCHEM, vol. 42, 1994, pages 239 - 249
- MURPHY S ET AL., METHODS CELL SCI, vol. 21, 1999, pages 31 - 38
- NAKAYAMADA S ET AL., J BIOL CHEM, vol. 278, 2003, pages 45368 - 45374
- NAKAYAMADA S ET AL., ARTHRITIS RHEUM, vol. 48, 2003, pages 1239 - 1248
- NEWSOME PN ET AL., HEPATOLOGY, vol. 40, 2004, pages 636 - 645
- NOONAN DM ET AL., J BIOL CHEM, vol. 266, 1991, pages 22939 - 22947
- NORGARD-SUMNICHT K; VARKI A, J BIOL CHEM, vol. 270, 1995, pages 12012 - 12024
- OTTERNESS IG ET AL., ARTHRITIS RHEUM, vol. 41, 1998, pages 2068 - 2076
- PAULUS W ET AL., J NEUROPATHOL EXP NEUROL, vol. 55, 1996, pages 528 - 533
- PERIDES G ET AL., J IOL HEM, vol. 267, 1992, pages 23883 - 23887
- POOLE AR ET AL., AGENTS ACTIONS SUPPL, vol. 39, 1993, pages 3 - 13
- ROBERTS CR.: "Proteoglycans. In: The Lung: Scientific Foundations", 1997, LIPPINCOTT-RAVEN PUBLISHERS, pages: 757 - 767
- SHAPIRO SD., BIOCHEM SOC TRANS, vol. 30, 2002, pages 98 - 102
- SHARMA B ET AL., J CLIN INVEST, vol. 102, 1998, pages 1599 - 1608
- SHINOMURA T ET AL., J BIOL CHEM, vol. 268, 1993, pages 14461 - 14469
- SPICER AP; MCDONALD JA.: "Eukaryotic Hyaluronan Synthases", 1999, SEIKAGAKU
- SUN M ET AL., CIRCULATION, vol. 107, 2003, pages 1046 - 1052
- TAKAHASHI I ET AL., J CELL SCI, vol. 111, 1998, pages 2067 - 2076
- THICKETT DR ET AL., SARCOIDOSIS VASE DIFFUSE LUNG DIS, vol. 18, 2001, pages 27 - 33
- TOOLE BP, CURR OPIN CELL BIOL, vol. 2, 1990, pages 839 - 844
- TUCKWELL DS; HUMPHRIES MJ, CRIT REV ONCOL HEMATOL, vol. 15, 1993, pages 149 - 171
- TURATO G; ZUIN R; SAETTA M, RESPIRATION, vol. 68, 2001, pages 117 - 128
- TURINO GM, AM REV RESPIR DIS, vol. 132, 1985, pages 1324 - 1334
- VAN KUPPEVELT TH ET AL., EUR J CELL BIOL, vol. 36, 1985, pages 74 - 80
- VILLAR ET AL., J CELL BIOCHEM, vol. 75, 1999, pages 665 - 674
- WARD ES ET AL., NATURE, vol. 341, 1989, pages 544 - 546
- WATANABE H ET AL., J BIOCHEM, vol. 124, 1998, pages 687 - 693
- WERNIG F ET AL., HYPERTENSION, vol. 41, 2003, pages 903 - 911
- WESTERGREN-THORSSON G ET AL., J CLIN INVEST, vol. 92, 1993, pages 632 - 637
- WIRTZ HR; DOBBS LG, RESPIR PHYSIOL, vol. 119, 2000, pages 1 - 17
- YAMAGATA M ET AL., J CELL SCI, vol. 106, 1993, pages 55 - 65
- ZAKO M ET AL., J BIOL CHEM, vol. 272, 1997, pages 9325 - 9331
- ZAKO M ET AL., J BIOL CHEM, vol. 270, 1995, pages 3914 - 3918
- ZHANG Y ET AL., J CELL BIOCHEM, vol. 73, 1999, pages 445 - 457
- ZHANG Y ET AL., J BIOL CHEM, vol. 273, 1998, pages 21342 - 21351
- ZIMMERMANN DR: "Proteoglycans: Structure, Biology and Molecular Interactions", 2000, MARCEL DEKKER, pages: 327 - 342
- ZIMMERMANN DR; RUOSLAHTI E, EMBO J, vol. 8, 1989, pages 2975 - 2981
- ZOU K ET AL., EUR J BIOCHEM, vol. 267, 2000, pages 4046 - 4053

#### Citation (search report)

- [A] WU YAOJIONG ET AL: "beta1-Integrin-mediated glioma cell adhesion and free radical-induced apoptosis are regulated by binding to a C-terminal domain of", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 277, no. 14, 5 April 2002 (2002-04-05), pages - 12301, XP002333545, ISSN: 0021-9258
- [A] WILKINS JOHN A ET AL: "Control of beta-1 integrin function: Localization of stimulatory epitopes", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 271, no. 6, 1996, pages 3046 - 3051, XP002333544, ISSN: 0021-9258
- [AD] GROSE RICHARD ET AL: "A crucial role of beta1 integrins for keratinocyte migration in vitro and during cutaneous wound repair", DEVELOPMENT (CAMBRIDGE), vol. 129, no. 9, May 2002 (2002-05-01), pages 2303 - 2315, XP002333543, ISSN: 0950-1991

- [A] BRAKEBUSCH CORD ET AL: "Genetic analysis of beta1 integrin function: Confirmed, new and revised roles for a crucial family of cell adhesion molecules", JOURNAL OF CELL SCIENCE, vol. 110, no. 23, December 1997 (1997-12-01), pages 2895 - 2904, XP002333546, ISSN: 0021-9533
- [AD] SUN MEI ET AL: "Temporal response and localization of integrins beta1 and beta3 in the heart after myocardial infarction: Regulation by cytokines.", CIRCULATION, vol. 107, no. 7, 25 February 2003 (2003-02-25), pages 1046 - 1052, XP009049771, ISSN: 0009-7322
- [A] HASSANIEH LOUBNA ET AL: "Generation of a monoclonal antibody to a cryptic site common to both integrin beta1 as well as gelatinase MMP9.", HYBRIDOMA AND HYBRIDOMICS, vol. 22, no. 5, 1 October 2003 (2003-10-01), pages 285 - 292, XP002333547, ISSN: 1536-8599

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